REMARKS

Status of the Claims

Claims 32-34 are pending and rejected.

Claim 32 has been amended.

New claims 35-46 have been added. Support for new claims 35-46 can be found throughout the application as originally filed including, for example, paragraphs [0032], [0033], [0095], [0142], [0200] and [0292].[1]

Upon entry of this amendment, claims 32-46 will be pending.

No new matter has been added.

Summary of the Invention

The present invention is directed to pharmaceutical compositions comprising anti-Vpr monoclonal antibodies and a pharmaceutically acceptable carrier, and to the use of such compositions in the treatment of individuals who have been exposed to and/or infected with HIV. Vpr protein is a biologically active HIV protein. As discussed in the specification, levels of Vpr in the individual are correlated with the progress of HIV. The presence of Vpr enhances the level of viral replication in HIV infected cells. (*See*, paragraph [0173]). Anti-Vpr antibodies are useful to inhibit Vpr's enhancement of viral replication in HIV infected cells. (*See*, paragraphs [0040] and [0175] for example.) Anti-Vpr antibodies raised against a fragment of Vpr having amino acids 2-12 inhibited Vpr's enhancement of viral replication in HIV infected cells. (*See*, paragraphs [0292].) According to the invention, a pharmaceutical composition comprising anti-Vpr antibodies that inhibit Vpr's enhancement of viral replication of HIV is administered to an individual infected with or exposed to HIV in order to inhibit the progression of HIV infection. (*See*, for example, paragraphs [0032], [0140], [0200] and [0315]).

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[1] Applicants note that while the as-filed application did not include paragraph numbering, the published application (United States Patent Application Publication 2003/0207252) does include paragraph numbering. Accordingly, paragraph numbers referred to in the present response are those in the published application.

Rejection under 35 U.S.C. § 102(b)

Claim 32 stands rejected under 35 U.S.C. §102(b) as allegedly anticipated by Sato *et al.* (Virus Genes, 4(4):303-312 (1990). The Office alleges that the Sato reference discloses "pharmaceutical compositions comprising HIV-1 Vpr-specific antibodies and an acceptable pharmaceutical carrier." (Office Action, pages 1-2).

Applicants note that claim 32 has been amended to recite that the anti-Vpr antibodies are monoclonal antibodies.

Sato *et al.* discusses the detection of the Vpr gene of human HIV-1 using "guinea pig antisera." Sato *et al.*, however, fails to disclose or even suggest the claimed invention, e.g., a pharmaceutical composition comprising anti-Vpr monoclonal antibodies.

Sato *et al.* also fails to disclose or suggest the subject matter of new claims 35 and 36, which are each dependent on claim 32. For example, Sato states that the composition used was based on "guinea pig antisera", not human antibodies (claim 35). Sato also fails to disclose a composition comprising monoclonal antibodies directed at amino acids 1-12 of the Vpr protein (claim 36).

Sato *et al.* similarly does not disclose or suggest the pharmaceutical compositions disclosed in new independent claim 37 and new claims 38-40 which depend from claim 37. In particular, Sato *et al.* does not disclose a pharmaceutical composition comprising anti-Vpr antibodies that inhibit Vpr enhancement of HIV replication in an amount effective to inhibit HIV replication in an HIV infected individual (claim 37). Sato *et al.* does not disclose a pharmaceutical composition comprising an amount of anti-Vpr monoclonal antibodies that inhibit Vpr enhancement of HIV replication effective to inhibit HIV replication in an HIV infected individual (claim 38) nor does Sato *et al.* disclose a pharmaceutical composition comprising an amount of anti-Vpr human monoclonal antibodies that inhibit Vpr enhancement of HIV replication effective to inhibit HIV replication in an HIV infected individual (claim 39). Sato *et al.* does not disclose a pharmaceutical composition comprising anti-Vpr antibodies that bind to a fragment of Vpr comprising amino acids 2-12 and inhibit Vpr enhancement of HIV replication in an amount effective to inhibit HIV replication in an HIV infected individual (claim 40).

Claim 32 as amended is not anticipated by Sato *et al.* Applicants respectfully request that the rejection of claim 32 under 35 U.S.C. §102(b) be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 33 and 34 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one having ordinary skill in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is asserted that the disclosure fails to provide adequate direction/guidance and working examples, that the claim breadth is excessive, and that the state of the art is unpredictable such that when considered *in toto*, it would require under experimentation to practice the claimed invention.

Applicants respectfully disagree and note that it is well established that the description is presumed to be enabled and that on order to sustain an enablement rejection under first paragraph of 35 U.S.C. § 112, the Examiner must establish using reasoning and evidence that those skilled in the art doubt the objective truth of Applicant's assertion that the claimed invention is enabled. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)." (M.P.E.P. § 2163).

In the present application, the Examiner has not met his burden. No evidence has been provided to support most of the positions taken in the official action, and for those in which any evidence is provided; all such evidence is directed at discussing the state of the art of a different field than the present invention, passive immunity using antibody compositions. No evidence is directed at discussing the state of the art of the field of the present invention, the use of antibodies to inactivate a biologically active protein. The evidence provided therefore does not raise issues as to the enablement of the claimed invention because the evidence is not relevant to the issue of enablement of the claimed invention. The enablement rejection set forth in the Official Action does not support or establish the conclusion that one skilled in the art would conclude that it would require under experimentation to practice the claimed invention. Failing to establish a *prima facie* case of lack of enablement, the claims must be accepted as enabled.

The invention is discussed above. The effect of Vpr on viral replication in HIV infected cells is discussed in detail in the specification such as in paragraphs [0173], [0183], [0184] and [0185]. The specification teaches the inhibition of this biological

activity of Vpr as a means to inhibit the progress of HIV infection in paragraphs [0040], [0051], [0052], [0142], [0175], [0190], [0200] and [0292].

It is asserted that the disclosure fails to provide adequate guidance pertaining to the structural and functional characteristics of the anti-Vpr antibodies. It is asserted that the skilled artisan would require knowledge of the epitope recognized, affinity, avidity, serum half life, bioavailability, clearance rates, sequestration of serum proteins and target levels before attempting to administer an antibody. No evidence is provided to support this assertion. No reasoning is provided to support the assertion. The assertion is a completely unsupported conclusion. In fact, one skilled in the art would conclude from the teachings in the specification that the claimed invention could be practiced without undue experimentation. All that would be necessary for one skilled in the art to practice the claimed invention as taught by the specification would be ordinary and routine experimentation, not undue experimentation. The specification reports that antibodies can interfere with Vpr's ability to enhance viral replication. One skilled in the art, armed with Applicants' disclosure and ordinary skill could practice the claimed invention. No evidence and no reasoning have been made to contradict this conclusion.

It is asserted that the claims are excessively broad. It is asserted that "the skilled artisan would need a purified, well characterized reagent" in order to practice the claimed invention and that the specification fails to provide sufficient disclosure of the properties for such an antibody compositions. No evidence is provided to support this assertion. No reasoning is provided to support the assertion. The assertion is a completely unsupported conclusion. Moreover, even if for arguments sake such unsupported assertion is accepted, no evidence or reasoning is provided to establish that undue experimentation would be required to obtain such an antibody composition. One skilled in the art, armed with Applicants' disclosure and ordinary skill could practice the claimed invention. No evidence and no reasoning have been made to contradict this conclusion.

It is asserted that the state of the art vis-à-vis the treatment of HIV infection using immunotherapeutics is characterized by unpredictability and frequent failure. The evidence to support this exclusively references discussing the problems and failures encountered in the development of HIV vaccines and passive immunity protocols. That is, each and every reference relied upon as evidence relates to problems associated with immunizing against HIV by protecting against or neutralizing infection. The invention is not directed to the art to which the state of the art analysis has been made. The present invention is directed toward inhibiting a biologically active protein involved in HIV

replication. All of the current HIV drugs are directed toward inhibiting a biologically active protein involved in HIV replication, albeit not Vpr. The evidence relied upon in support of the rejection is directed at failed attempts to prevent infection by neutralizing infection either using vaccines which induce immune responses that kill infected cells and/or generate antibodies that neutralize viral particles or using passive immunity protocols which administer to infect individuals antibodies produced outside the body to neutralize viral particles. The claimed invention is not related to conferring immunity against infection. The claimed invention is related to inhibiting viral replication by inhibiting activity of a viral protein. The specification reports the ability of Vpr to enhance viral replication and that antibodies interfere with this activity. The specification discloses inhibiting Vpr activity to reduce the progress of the HIV infection. No evidence and no reasoning have been provided to raise doubt that the claimed invention is enabled. One skilled in the art, armed with Applicant's disclosure and ordinary skill could practice the claimed invention.

It is asserted that because of the alleged "unpredictability of the art and nature of the invention, the skilled artisan would clearly require suitable working examples of the claimed invention before contemplating practicing the invention on an infected patient." This conclusory statement is offered without evidence or reasoning. Moreover, there is no standard or requirement relating to requirements as to what is needed before the skilled artisan would contemplate practicing the claimed invention. The standard is whether or not the skilled artisan can practice the claimed invention in view of the disclosure in the specification. There is nothing in the record that supports a conclusion that the skilled artisan would expect that undue experimentation would be required to practice the invention due to the lack of working examples.

When all of the *Wands* factors are consider together and the assertions made by the examiner are viewed in the aggregate, it is clear that no prima facie case has been made to support an enablement rejection. Of the four factors considered in the analysis offered in the Official action, three are mere conclusory statements without any supporting evidence or reasoning. The evidence provided for the factor relating to the state of the art does not pertain to the claimed invention and offers no support to question the enablement of the invention. The specification clearly describes the claimed invention as inhibiting a biologically active protein, not a vaccine and not a passive immunity protocol. This is clear to those skilled in the art. The evidence questions the predictability of vaccines and passive immunity protocols. Thus, the only evidence or

reasoning offered beyond unsupported conclusory statements is directed at the state of the vaccine and passive immunity art, not the state of the art of the claimed invention.

No *prima facie* case of non-enablement has been made. To the extent that there is evidence on the record, it does not support a finding that the claimed invention, as described in the specification, is not enabled. The specification fully supports a finding that the claimed invention is enabled. One skilled in the art would not conclude that undue experimentation would be necessary to practice the claimed invention.

The assertions that have been made in the Official Action alleging that the claimed invention is not enabled are either completely unsupported by any evidence or the evidence that has been provided is irrelevant to the issue for which it has been cited. For the record, Applicants vigorously disagree with the conclusions set forth in the Official Action. The specification provides adequate support to allow one having ordinary skill in the art to practice the invention without undue experimentation. The information asserted to be needed, to the extent it is needed, can be readily and routinely ascertained without undue experimentation. One skilled in the art would conclude that the specification fully supports the breadth of the claims. The state of the art is sufficiently predictable to provide a reasonable expectation of success and the disclosure and data reported in the specification is sufficient to support a conclusion that one skilled in the art could practice the invention without undue experimentation.

However, unless and until evidence or reasoning is offered to support the conclusory statements offered in the Official Action, no *prima facie* case of non-enablement is made and the assumption remains that the specification enables the claimed invention. Under the requirements of the law, the examiner has not met the requirements needed to establish a *prima facie* case and the burden has not shifted to the applicant to present a rebuttal.

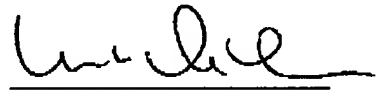
There is no evidence that would raise doubts as to the enablement of the present invention. The Office has provided no evidence supporting a rejection of the claims. Accordingly, the Examiner must accept the objective truth of Applicants' assertion.

The claimed invention is enabled. When all of the evidence is viewed in its totality one skilled in the art would accept the object truth of Applicant's assertion of enablement. Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Conclusion

Claims 32-46 are in condition for allowance. Applicants respectfully request that 32-46 be allowed. A notice of allowance is earnestly solicited.

Respectfully submitted,



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